CARE TEAM FORUM®

OPTIMIZING BIOLOGIC THERAPY IN CHILDREN WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

Provided by
RMEI Medical Education, LLC

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This activity is supported by an educational grant from Sanofi and Regeneron Pharmaceuticals.

Agenda

Type 2 Inflammation in Atopic Dermatitis and the Atopic March

Panel Discussion

Current and Emerging Biologics for Moderate-to-Severe Atopic Dermatitis in Children

Panel Discussion

Interprofessional Management of Comorbidities in Children with Moderate-to-Severe Atopic Dermatitis

Panel Discussion

Type 2 Inflammation in Atopic Dermatitis and the Atopic March

Pathophysiology

- AD is not just skin deep and it's not just a structural disease
- It's an immunologic disease that involves multiple players in the immune system
- At the center of the pathophysiology of AD is the IL-4

Beck LA, et al. *JID Innov.* 2022;2(5):100131.

Role of IL-4 and IL-13 in AD

- **Th2 Differentiation**
  - IL-4 promotes T-helper cell differentiation from Th0 to Th2
  - IL-4 also activates cells like mast cells and recruitment of basophils
- **Similar but not identical**
  - Though IL-4 and IL-13 have overlapping functions, they are not identical

Beck LA, et al. *JID Innov.* 2022;2(5):100131.

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Christy

What was your daughter's experience with AD and asthma in early life and how did that evolve over the course of time?

Current and Emerging Biologics for Moderate-to-Severe Atopic Dermatitis in Children

Christy

When did you notice your daughter's AD taking a turn for the worse?

Describe how severe it became and your thoughts on how it was initially managed?

Conventional Therapies

Non-Pharmacologic Therapy

Phototherapy
Wet Wrap Therapy
Bleach Baths
Moisturizers

Topical Therapy

Topical Corticosteroids (TCS)
Topical Calcineurin Inhibitors (TCI)
Crisaborole (PDE-4i)

Conventional Systemic Therapy

Systemic Corticosteroids
Cyclosporine
Methotrexate
Mycophenolate mofetil
Azathioprine

Dupilumab Over Time in Moderate-Severe Atopic Dermatitis

March 2017
First Approval: Adults

2017

2019

March 2019
Approval in ages 12 to 17

May 2020
Approval in ages 6 to 11 years

2020

2022

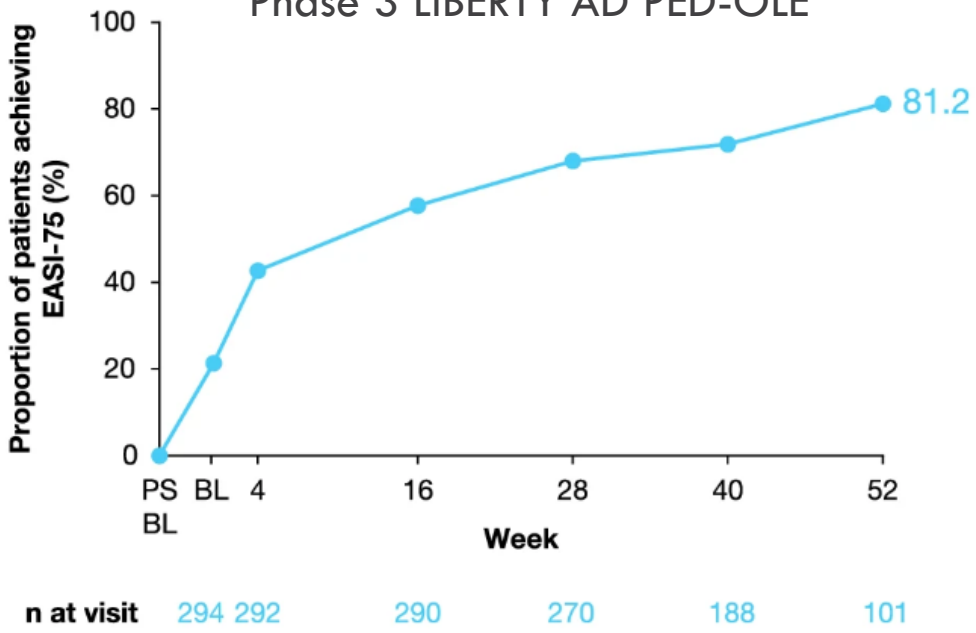
June 2022
Approval in ages 6 months to 5 years

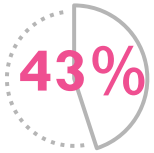
Stewart J. www.drugs.com

Dupilumab

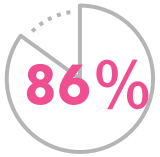
Efficacy in Ages 12 to 17 Years

Phase 3 LIBERTY AD PED-OLE



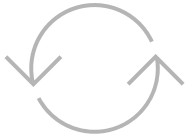


of patients achieved an investigator global assessment of 0/1 (clear/almost clear skin)



86% of patients achieved ≥6-point improvement in the children's dermatology QoL index

Most patients required up-titration from q4weeks to q2weeks

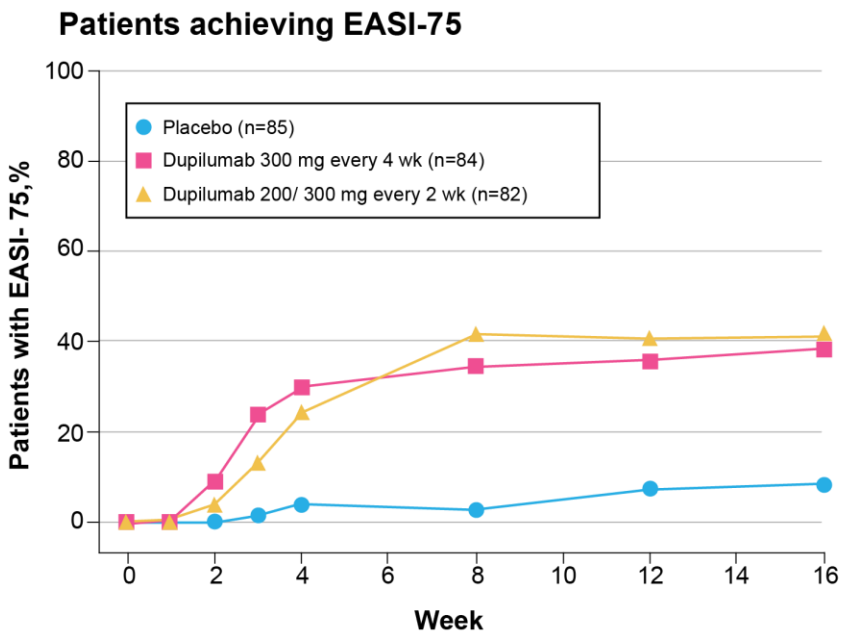


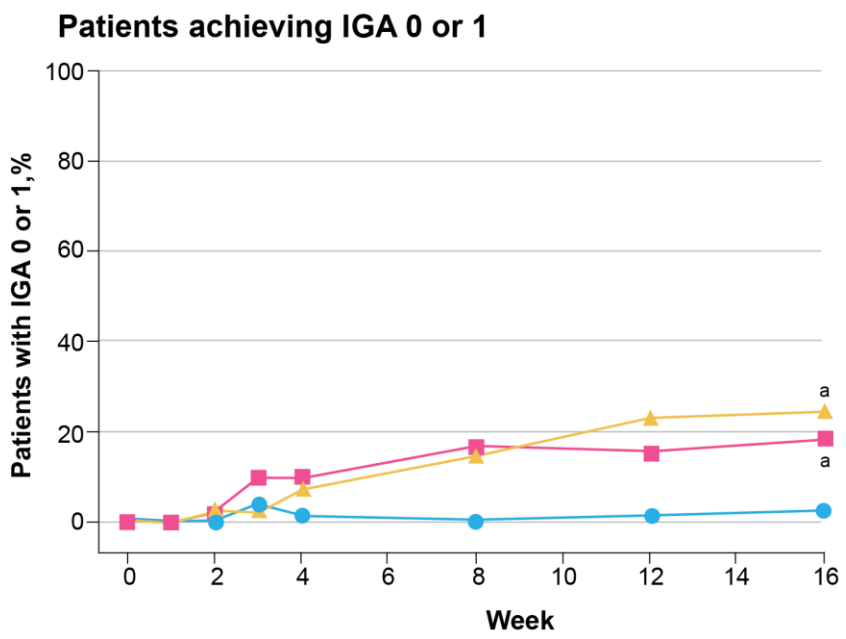
Discontinuing patients experienced AD recurrence

Blauvelt A, et al. *Am J Clin Dermatol*. 2022;23(3):365-383.

Dupilumab

Efficacy in Ages 12 to 17 Years





- Patients with comorbid asthma or allergic rhinitis showed numeric improvement in control/ symptoms
- IgE concentrations for specific food and aeroallergens were significantly suppressed
- Statistically/clinically significant improvements were observed in signs/symptoms of AD, itch, sleep, and QoL

Simpson EL, et al. *JAMA Dermatol.* 2020;156(1):44-56.

Dupilumab

Efficacy in Ages ≥6 Months to 5 Years

LIBERTY AD PRESCHOOL

Week 16: Patients Achieving IGA 0-1

Placebo 4%
Dupilumab 28%
P<.0001

Overall Adverse Events

Dupilumab 64%
Placebo: 74% (78 patients)

Week 16: Patients Achieving EASI-75

Placebo 11%
Dupilumab 53%
P<.0001

Conjunctivitis Incidence

Dupilumab: 5%
Placebo: 0%

N=162, Dupilumab + TCS: 83, Placebo: 79

Paller AS, et al. *Lancet. 2022*;400(10356):908-919.

Panel Discussion

What safety concerns do patients and providers have with dupilumab and how do you work as a team to mitigate them?

In your practice, what seems to be the main driver for discontinuing biologic therapy?

Panel Discussion

In your clinics, how do you safely transition children from immunomodulators to dupilumab, if required?

Approach to Transition

	Week 0 to 8	Disease Control Week 8 - …	No Disease Control
CsA	Maintain Dose	Reduce dose every 2 weeks by 25% of starting dose	If current dose was used for roughly <8 weeks, continue immunosuppressant at the same dose for another 4 weeks If current dose was used for roughly >8 weeks, consider continuation of concomitant immunosuppressant at the lowest possible, effective dose on the long term and/or consider discontinuation of dupilumab treatment
MTX AZA MPA MMF	Maintain Dose	Every 4 weeks reduce dose by 50% of starting dose	

de Wijs LEM, et al. *J Eur Avad Dermatol Venereol.* 2021;35(3):e221-e223.

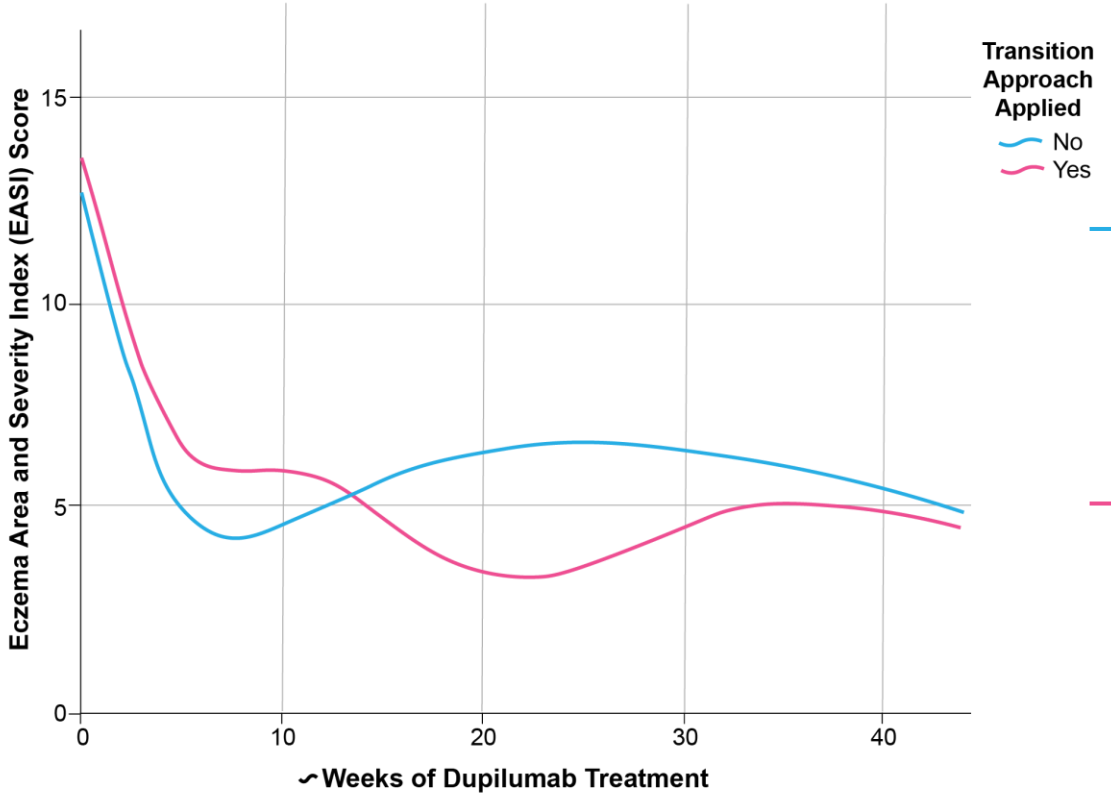
Approach to Transition

	Week 0 to 8	Disease Control Week 8 - …	No Disease Control
CsA	*For Example:* 100 mg BID for weeks 0 to 8	*For Example:* 75 mg BID wk 8 to 10 50 mg BID wk 10 to 12 25 mg BID wk 12 to 14 d/c CsA on wk 14	
MTX AZA MPA MMF	*For Example:* MTX 15 mg weekly weeks 0 to 8	*For Example:* 7.5 mg/wk 8 to 12 d/c MTX wk 12	

de Wijs LEM, et al. *J Eur Avad Dermatol Venereol.* 2021;35(3):e221-e223.

Approach to Transition

DISEASE SEVERITY OF PATIENTS WITH AND WITHOUT THE USE OF THE PROPOSED TRANSITION APPROACH



- Patients with AD (n=61) who discontinued immunosuppressants at the start or in the first 12 to 14 weeks of dupilumab treatment
- Patients with AD (n=44) with concomitant systemic immunosuppressants that were slowly tapered and then discontinued after at least 12 to 14 weeks of dupilumab treatment, according to the transition approach described

de Wijs LEM, et al. *J Eur Avad Dermatol Venereol.* 2021;35(3):e221-e223.

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Christy

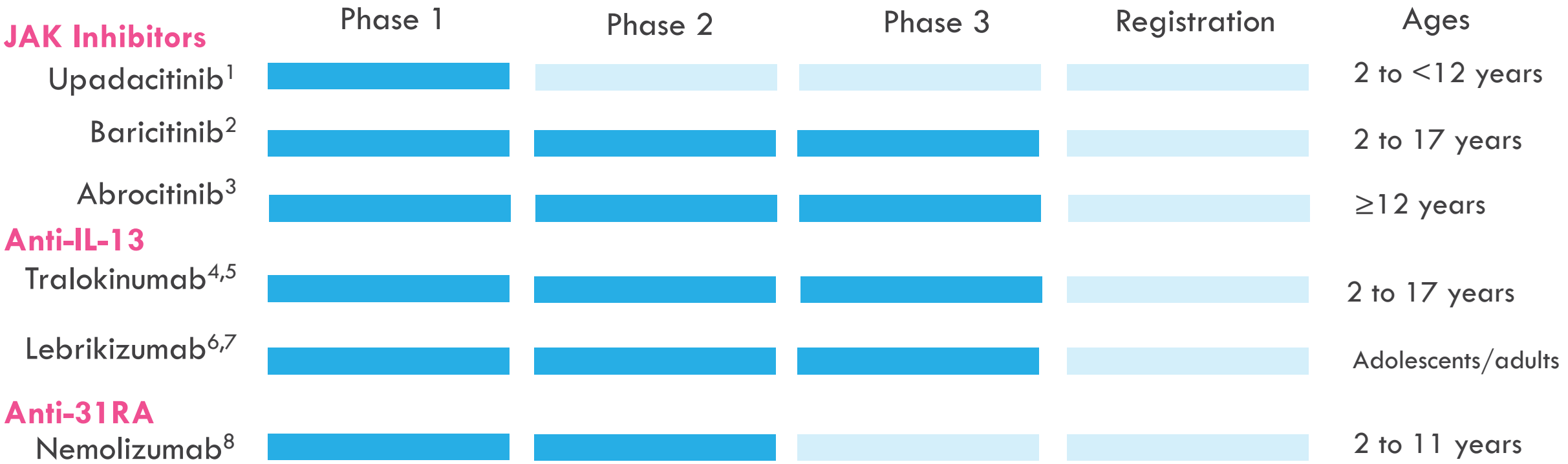
Your daughter was eventually placed on dupilumab. Walk us through your first day at the multidisciplinary clinic and how that was for you and your daughter.

Panel Discussion

Are there any special safety/monitoring considerations to be taken when prescribing dupilumab to infants?

What challenges do you encounter that are unique to infants when it comes to *administering* dupilumab and what tips do you have to help overcome them?

Emerging Therapies for Children



1. NCT03646604; 2. NCT03952559; 3. NCT03422822; 4. NCT05388760;
5. NCT03526861; 6. NCT05372419; 7. NCT05369403; 8. NCT04921345.

JAK Inhibitors

Emerging Therapies for Children

Phase 3
BREEZE-AD-PEDs

N=483
Children/adolescents
(2 to 17 years)

Data in Pediatrics: Baricitinib

Week 16: Patients achieving IGA 0-1 *and*
≥2-point improvement from baseline

*Baricitinib 2 mg in children <10 years and baricitinib 4 mg in children 10 to 17 years.

NCT03952559; *Torrelo A,* et al. Presented at: European Academy of Dermatology and Venereology; September 7-10, 2022; Milan, Italy.

JAK Inhibitors

Emerging Therapies for Children

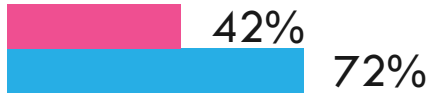
Phase 3
JADE TEEN[1,2]

N=285
Adolescents
(12 to 17 years)

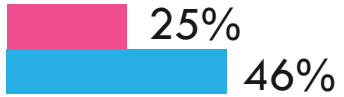
Data in Pediatrics: Abrocitinib

Currently approved in the UK for ages ≥12 years[3]

Week 12: Patients Achieving ESAI 75



Week 12: Patients Achieving IGA 0-1



1. Bourkas AN, et al. *SAGE Open Med Case Rep.* 2022;10:2050313X221138452; 2. Eichenfield LF, et al. *JAMA Dermatol.* 2021;157(10):1165-1173. 3. Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2022;36(9):1409-1431;

Safety considerations: JAK Inhibitors

Class-wide Boxed Warning: Risks for thrombosis, major adverse cardiovascular events, and all-cause mortality[1]

Phase 3 BREEZE-AD PEDS (Baricitinib)[2]

Overall Treatment-Emergent Adverse Events

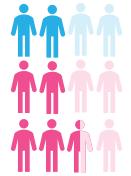
- Overall: ~50% both groups
- No severe adverse effects
- No new safety signals
- No cases of DVT, PE, or other AESIs
- Some cases of elevated creatinine phosphokinase levels not due to muscle injury; possible increase in low-density cholesterol level

*One Phase 3 study of patients aged ≥13 years in Japan.

Phase 3 JADE TEEN (Abrocitinib)[3]

Overall Treatment-Emergent Adverse Events

Placebo: 52.1%
Abrocitinib 100 mg: 56.8%
Abrocitinib 200 mg: 62.8%



Adverse Events of Special Interest

AE of Special Interest	N	Group
Cutaneous herpes zoster	1	Abrocitinib
Herpes simplex	1	Abrocitinib
Oral herpes	3	Abrocitinib
Conjunctivitis	1	Placebo
Acne	8 1	Abrocitinib Placebo

1. Daniele SG, et al. *J Drugs* Dermatol. 2022;21(12):1298-1303; 2. Torrelo A, et al. Presented at: European Academy of Dermatology and Venereology; September 7-10, 2022; Milan, Italy; 3. Eichenfield LF, et al. *JAMA Dermatol*. 2021;157(10):1-9.

Anti-IL-13

Emerging Therapies for Children

Phase 3
ECZTRA 6

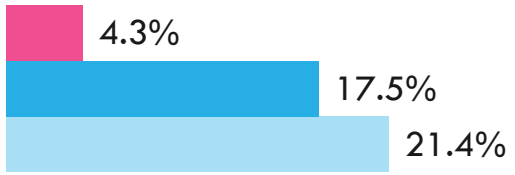
N=289
Adolescents

Data in Pediatrics: Tralokinumab

Currently approved for use in adults with moderate-to-severe AD

Week 16: Patients Achieving EASI 75

Placebo
Tralokinumab 300 mg *P*=.002
Tralokinumab 150 mg *P*<.001



Week 16: Patients Achieving IGA 0-1

Placebo
Tralokinumab 300 mg *P*=.001
Tralokinumab 150 mg *P*<.001

Paller A, et al. Presented at: The 4th Annual Revolutionizing Atopic Dermatitis Virtual Conference; April 9-11, 2022.

Safety Considerations: Monoclonal Antibodies

Anti-IL-13

Increased risk of conjunctivitis based on a systematic review and meta-analysis of RCTs in adults with AD[1]

Lebrikizumab: 6.3%
Tralokinumab: 6.2%

Phase 3 ECZTRA 6 (tralokinumab, adolescents)[2]

Placebo: 2.1%
Tralokinumab: 3.1% to 4.1%

Anti-IL-31RA

Systematic review and meta-regression analysis of RCTs in adults with AD[3]*

Most frequently reported AEs were:

- Skin or subcutaneous tissue disorders including nasopharyngitis (10% to 32.7%)
- Exacerbated AD (15% to 28.1%)

*One Phase 3 study of patients aged ≥13 years in Japan.

1. Zhang Y, et al. *Front Immunol.* 2022;13:923362.doi:10.3389 eCollection 2022; 2. Paller A, et al. Presented at: The 4th Annual Revolutionizing Atopic Dermatitis Virtual Conference; April 9-11, 2022; 3. Liang J, et al. *Front Immunol.* 2022;13:825312.doi: 10.3389 eCollection 2022.

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Panel Discussion

Where do you see JAK inhibitors and IL-31 inhibitors playing a role in the treatment of AD in children?

Will these be reserved for patients with refractory to dupilumab?

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Panel Discussion

As the armamentarium of IL-13 targeting mAbs grows, how are these new agents designed to be different from dupilumab, which dually targets IL-4 and IL-13?

Is there expected to be a clinical difference in safety, efficacy, or patient selection?

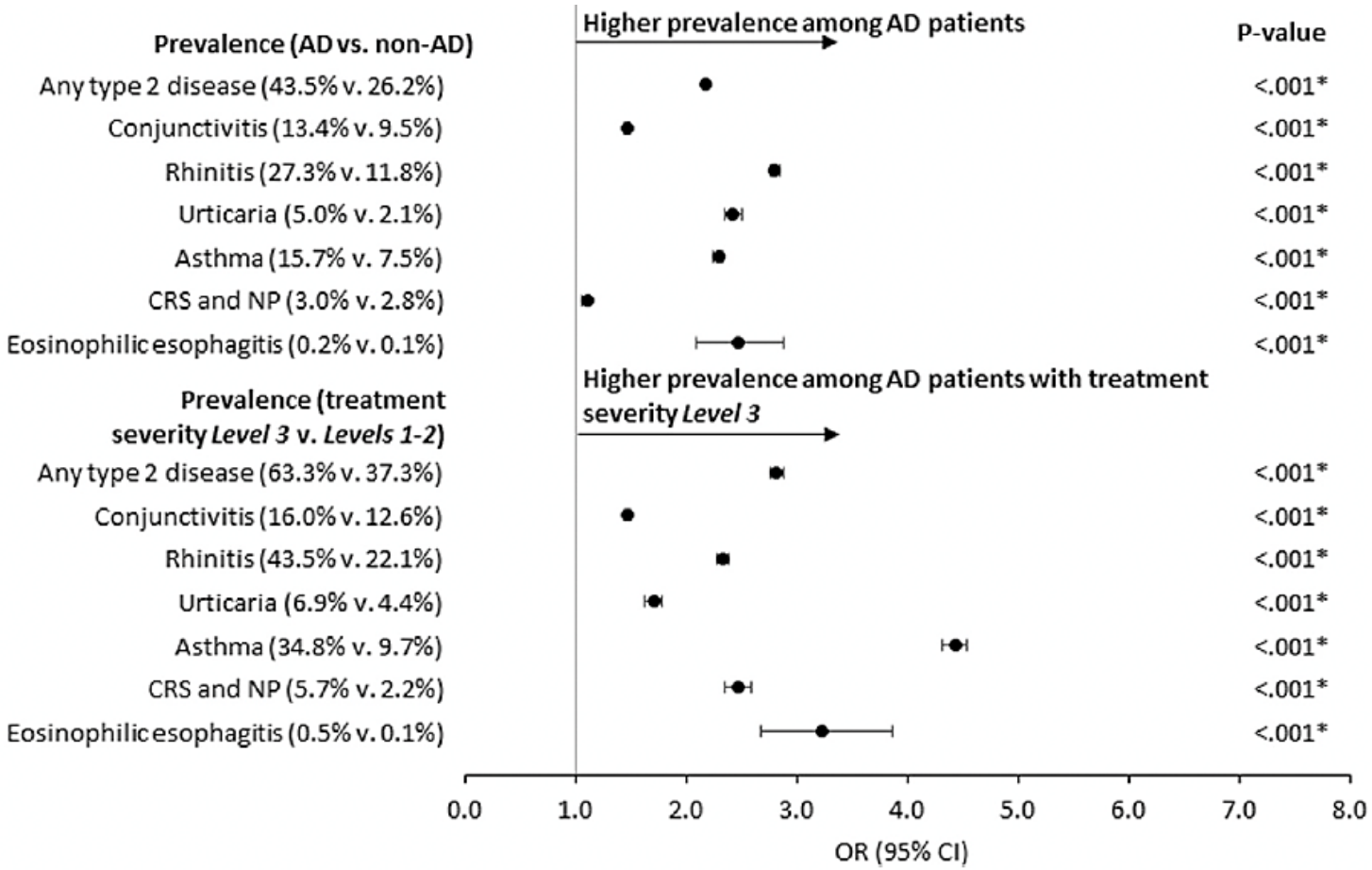
Interprofessional Management of Comorbidities in Children with Moderate-to-Severe Atopic Dermatitis

Common Atopic Comorbidities

>2xs

Patients with AD were **more than twice as likely** than patients without AD to be diagnosed **with an atopic comorbidity**

Prevalence of additional atopic comorbidities **increased with increasing severity of AD**



Paller AS, et al. *J Am Acad Dermatol*. 2022;86(4):758-765.

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Panel Discussion

How do you work as a team to effectively manage atopic comorbidities in pediatric patients?

Psychosocial Issues

- Sleep-related impairment[1]
- Sleep-related anxiety[1]
- ADD/ADHD[2]
- Autism[2]
- Sleep-related depression[1]
- Sleep-related inattention[1]
- Emotional/ behavioral difficulties[2,3]
- Bullying[4]
- Sleep-related fatigue[1]
- Sleep-related impulsivity[1]
- Feelings of frequent worry[2]
- Family disruption[5]

1. Fishbein AB, et al. *J Allergy Clin Immunol Pract*. 2021;9(8):3120-3129; 2. Hou A, et al. *Pediatr Dermatol*. 2021;38(3):606-612; 3. Manjunath J, et al. *Dermatitis*. 2022;33(6S):S52-S60; 4. Stingeni L, et al. *J Asthma Allergy*. 2021;14:919-928; 5. Eichenfield LF, et al. *Paediatr Drugs*. 2022;24(4):293-305.

Panel Discussion

How do you work as an interprofessional and multidisciplinary team at your institution to identify and address the *psychosocial burden* associated with AD in children and their families?

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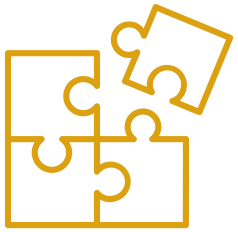
Christy

During doctor visits, you are often required to complete forms that ask about your daughter's quality of life with eczema.

What did you learn about your daughter and her life with AD as you filled these forms out together?

Coordinated and Structured Multidisciplinary Care Teams are Helpful to Manage Complex Patients



They follow a structured and coordinated approach to provide holistic patient care

The team can include dermatologists, nurses/medical assistants/physician assistants, allergists, pharmacists, psychologists/psychiatrists, nutritionists, pulmonologists, or departments to which patients can easily be referred for testing, diagnosis, management, and support

An important aspect is identifying a primary point of contact within the team for connecting, communicating, and providing proper triage of care

Guttman-Yassky E, et al. *Clin Exp Dermatol*. 2022;47(2):303-311.

Panel Discussion

What are some best practices that you employ at your institution for involving *all members of the healthcare team* in the care of children with AD?

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Christy

What was your experience meeting with the different members of the interprofessional care team at the clinic?

What do you recommend to improve the experience and make it a little less overwhelming?

Benefits of Interprofessional Care: Multidisciplinary Educational Program in Norway

Providers in the Educational Program:

Patient Organizations
Caregiver Representative
Dermatologist
Nurse
Psychologist
Social Worker

Three months after attendance, there was improvement in:

Family QoL

Dermatitis Family Impact

Baseline 6.8
After 3 months 9.6
P<.001

AD Severity

Patient Oriented – Scoring AD

Baseline 24.6
After 3 months 38.5
P<.001

Reduced Fear of Topical Steroids

Lundborg M, et al. *BMC Dermatol*. 2020;20(1):20.

Panel Discussion

What challenges and successes have you experienced in providing interprofessional care for children with AD and their caregivers?

Panel Discussion

What best practices are recommended for patient and caregiver education?

Christy

What was your experience with education on AD and its treatment?

What did you find the most impactful and relevant to your needs?

Summary

- Type 2 inflammatory cytokines are involved in the pathogenesis of moderate-to-severe AD and other atopic diseases and are the target of current and emerging biologics.
- Emerging immune-directed therapies for the treatment of moderate-to-severe AD in children include, biologics targeting IL-13 and IL-31, and small molecules targeting JAK.
- The interprofessional care team can play an important role in managing the complex needs of children with moderate-to-severe AD and comorbidities.